REMARKS

Applicants submit an abstract in the response contained herein and on a separate piece of paper attached as Appendix A.

Claims 35-46 are pending in this application. Claims 35 and 43 have been amended to clarify the scope of the present invention without prejudice and acquiescence. A marked up version of the claims is attached to this response as Appendix B. For the convenience of the Examiner, Applicants have also included a copy of all pending claims as Appendix C. No new matter has been added.

The issues outstanding in this application are as follows:

- The Oath or Declaration has been objected to as allegedly not containing a priority claim to U.S. provisional application 60/053,211 and Swedish application 9704170-1.
- The Application has been objected to as allegedly not containing an abstract.
- The Specification has been objected to as allegedly containing informalities in the references cited.
- Claims 35-46 have been rejected by the Examiner under 35 U.S.C. § 112, second paragraph as allegedly being indefinite.
- Claims 35-46 have been rejected by the Examiner under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter which was not described.
- Claims 35, 37-41 and 45-46 have been rejected by the Examiner under 35 U.S.C. § 103(a) as being allegedly being unpatentable over Belfrage et al. (Immunology, 90:183, 1997).
- Claims 35, 37-38, 41 and 45-46 have been rejected by the Examiner under 35 U.S.C. § 102(b) as being allegedly being anticipated by Lando et al., (J. Immunol., 157:2857, 1996).

- Claims 35 and 37-46 have been rejected by the Examiner under 35 U.S.C. § 103(a) as being allegedly being unpatentable over Belfrage et al. in view of Abrahmensen et al. (WO 96/01650) and Antonsson et al. (WO 97/36932).

- Submission of Belfrage thesis (1996) and Belfrage et al., (1997b) are required.

Applicants respectfully traverse the outstanding rejections and objections, and Applicants respectfully request reconsideration and withdrawal thereof in light of the amendments and remarks contained herein.

I. Priority claim is correct.

The Office has indicated that the Oath or Declaration was allegedly defective because it did not contain a priority claim to U.S. provisional application 60/053,211 and Swedish application 9704170-1. Applicants respectfully traverse.

Applicants submit herewith in lieu of a newly executed Oath or Declaration an Application Data Sheet in accordance with 37 CFR § 1.76 claiming priority to both the U.S. provisional application and Swedish application. Thus, Applicants respectfully request that the objection be withdrawn.

II. Abstract is present.

The Office has indicated that the Application has been objected to as allegedly not containing an Abstract. Applicants respectfully traverse.

Applicants submit herewith on a separate piece of paper attached as Appendix A an Abstract. Thus, Applicants respectfully request that the objection be withdrawn.

III. The References cited are correct.

The Office has indicated that the Specification has been objected to as allegedly not containing informalities in the references cited. Applicants respectfully traverse.

Applicants have amended the indicated references on pages 61-65 of the Specification. A marked version of the amendments contained herein can be found in Appendix B. Thus, Applicants respectfully request that the objection be withdrawn.

IV. Claims 35-46 are definite under 35 U.S.C. § 112, second paragraph

Claims 35-46 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regards as the invention. Applicants respectfully traverse.

Applicants have amended claim 35 to recite what the targeting moiety is targeting without prejudice or acquiescence. Applicants have also amended claim 43 to recite "seroreactivity in human sera" without prejudice or acquiescence. In light of these amendments, Applicants request that the rejection be removed.

V. Claims 35-46 are described under 35 U.S.C. § 112, first paragraph

Claims 35-46 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse.

Applicants have amended claim 35 to recite what the targeting moiety is targeting without prejudice or acquiescence. In light of these amendments, Applicants request that the rejection be removed.

VI. Claims 35, 37-41 and 45-46 are not obvious under 35 U.S.C. § 103(a).

Claims 35, 37-41 and 45-46 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Belfrage et al. The Action states that Belfrage et al. teaches coadministration of a wild type superantigen conjugated to a targetting antibody and using

IL-2 to increase the immunotherapeutic killing of cancer cells. Applicants traverse and respectfully request withdrawal of the Belfrage et al. reference.

Applicants assert that they are the authors of the Belfrage et al. reference cited against the present invention. Applicants submit a Declaration by Terje Kalland (paragraphs 4 and 6), which states that the Belfrage et al. reference describes applicants' work. Thus, in light of the Declaration by Terje Kalland, Applicants have provided sufficient evidence to remove Belfrage et al. as a reference, and respectfully request that the rejection be withdrawn. *In re Katz*, 687 F.2d 450, 215 USPQ 14 (CCPA).

VII. Claims 35, 37-38, 41 and 45-46 are not anticipated under 35 U.S.C. § 102(b).

Claims 35, 37-38, 41 and 45-46 were rejected under 35 U.S.C. § 102(b) as being anticipated by Lando et al. The Action states that Lando et al. teaches coadministration of a superantigen conjugated to a targetting antibody and of IL-2 in a culture system in which the target cells express a tumor antigen. Applicants traverse and respectfully request withdrawal of the Lando et al. reference.

Applicants assert that they are the authors of the Lando et al. reference cited against the present invention. Applicants submit a Declaration by Terje Kalland (paragraphs 5 and 6), which states that the Lando et al. reference describes applicants' work. Thus, in light of the Declaration by Terje Kalland, Applicants have provided sufficient evidence to remove Lando et al. as a reference, and respectfully request that the rejection be withdrawn. *In re Katz*, 687 F.2d 450, 215 USPQ 14 (CCPA).

VIII. Claims 35 and 37-46 are not obvious under 35 U.S.C. § 103(b).

Claims 35, 37-41 and 45-46 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Belfrage et al. in view of Abrahmsen et al. (WO 96/01650) and Antonsson et al. (WO 97/36932). The Action states that it would have been obvious to employ the targeted superantigens that were modified and taught by Abrahmsen et al. and Antonsson et

al. in view of Belfrage. Applicants traverse and respectfully request withdrawal of the Belfrage et al. reference and Antonsson et al. (WO 97/36932) reference.

Obviousness can only be established by combining or modifying the references of the prior art to produce the claimed invention when there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

Applicants assert that sufficient evidence has been provided in the 1.132 Declaration, which is provided herein, to remove Belfrage et al. as a reference. Yet further, the Action states that WO 97/36932 post-dates the provisional application. Applicants assert that the amended Application Data Sheet provided herein contains corrects the priority information to provide an effective filing date of July 21, 1997, which is the date of the provisional application. In light of the effective filing date being July 21, 1997, Applicants assert that the WO 97/36932 is not prior art against the present invention because WO 97/36932 was published on October 9, 1997. Thus, Applicants respectfully request that the primary reference, Belfrage et al., and the secondary reference WO 97/36932 be removed.

Thus, the only reference that is available as prior art is WO 96/01650, which only teaches a conjugate of a superantigen and a targeting moiety, such as an antibody. WO 96/01650 does not teach nor suggest using cytokines to enhance the immunotherapeutic effectiveness of the superantigen conjugate.

Even if both WO 97/36932 and Belfrage et al. were available as prior art references, there is no teaching nor suggestion to produce the claimed invention of using all three components, a superantigen, a targeting moiety and an immune stimulator.

Therefore, applicants respectfully request withdrawal of the § 103(a) obviousness rejection.

IX. Submission of References.

The Action has requested that Applicants provide a copy of the Belfrage thesis (1996) and Belfrage et al. (1997b). Yet further, the Action has stated that the fee and certification requirements of 37 CFR § 1.97 are waived for these documents. Thus, Applicants submit herewith a copy of each reference.

CONCLUSION

Claims 35-46 are now pending in this application. Claims 35 and 43 have been amended without prejudice and acquiescence. Applicants have attached a marked version of the pending claims as Appendix A to show changes made.

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 06-2375, under Order No. 10001907 from which the undersigned is authorized to draw.

Dated:

Respectfully submitted,

By

David L. Fox
Registration No.: 40,612
FULBRIGHT & JAWORSKI L.L.P.
1301 McKinney, Suite 5100
Houston, Texas 77010-3095
(713) 651-5151
(713) 651-5246 (Fax)

APPENDIX A

ABSTRACT

A method for inactivating target cells in the presence of T cells by bringing the two types of cells in contact with a superantigen (SAG) in the presence of an immune modulator, characterized in that at least one of the superantigen and the immune modulator is in the form of a conjugate between a "free" superantigen and a moiety. The superantigen conjugate is preferably a triple fusion protein. A targeted immune modulator, characterized in that it is a conjugate between a targeting moiety (T) and a modified immune modulator (IM).

APPENDIX B
VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

Page 60, line 2

***Bamborough et al.** (1994) Structure 2:839-51.

page 60, lines 21-22

***Belfrage et al** (1997b) Prevention of superantigen induced tolerance in vivo by IL-2 treatment. ~~Submitted 1996~~Cancer Immunol. Immunother. 44:77-82.

Page 60, line 23

***Berndt et al** (1994) Biochemistry 33:6571-7.

Page 61, line 20

***Collins et al** (1988) Proc. Natl. Acad. Sci. USA 85:7709-13.

page 62, lines 20-21

Hansson J et al (1997) Proc. Natl. Acad. Sci. –U.S.A. 94 ~~(in press)~~:2489-94.

Page 65, line 6

***Zurawski et al** (1993) EMBO J. 12:5113-9.

In the Claims:

35. (Amended) A method for inactivating a target cell in the presence of T cells comprising bringing the target cell and a T cell in contact with a superantigen in the presence of an immune modulator wherein at least one of the superantigen and immune modulator is conjugated to a targeting moiety that targets the target cell.

43. (Amended) The method of claim 1, wherein the superantigen is modified to have decreased seroreactivity ~~or immunogenicity~~ in human sera compared to the corresponding wild type superantigen.

APPENDIX C
CLAIMS PENDING AS OF OCTOBER 11, 2002

35. A method for inactivating a target cell in the presence of T cells comprising bringing the target cell and a T cell in contact with a superantigen in the presence of an immune modulator wherein at least one of the superantigen and immune modulator is conjugated to a targeting moiety that targets the target cell.

36. The method of claim 35, wherein the superantigen and immune modulator are both conjugated to the same targeting moiety, the conjugate being a triple conjugate.

37. The method of claim 35, wherein the superantigen and targeting moiety are conjugated.

38. The method of claim 35, wherein the immune modulator is not conjugated to the targeting moiety.

39. The method of claim 35, wherein the target cell is inactivated in vivo in an individual having a disease associated with the target cell.

40. The method of claim 39, wherein the disease is cancer.

41. The method of claim 35, wherein the targeting moiety is slected from the group consisting of an antibody, an antigen-binding fragment of an antibody, an Fab fragment of an antibody, an Fab_2 fragment of an antibody, or a single chain antibody.

42. The method of claim 35, wherein the superantigen is modified to have a decreased ability to bind to MHC class II antigen compared to the corresponding wild type superantigen.

43. The method of claim ~~1~~ 35, wherein the superantigen is modified to have decreased seroreactivity in human sera compared to the corresponding wild type superantigen.

44. The method of claim ~~1~~ 35, wherein the superantigen is chimeric comprising sequences derived from two or more wild type superantigens.

45. The method of claim ~~1~~ 35, wherein the immune modulator is selected from the group consisting of cytokines, chemokines, and extracellular parts of lymphocyte bound receptors and ligands.

46. The method of claim ~~1~~ 35, where in the immune modulator is IL-2.